UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/679,362	10/07/2003	Ming-Hui Wei	CL001062-CON	5605

25748 7590 11/03/2006

CELERA GENOMICS
ATTN: WAYNE MONTGOMERY, VICE PRES, INTEL PROPERTY
45 WEST GUDE DRIVE
C2-4#20
ROCKVILLE, MD 20850

EXAMINER	
SEHARASEYON, JEGATHEESAN	
ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 11/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/679,362	WEI ET AL.	
	Examiner	Art Unit	
	Jegatheesan Seharaseyon, Ph.D	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) *6 and 12-16* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 7-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *07 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Office Action mailed 8/31/06 has been vacated to correct typographical errors. The references provided on PTO-892 of 8/31/06 will not be resent. In addition, the Appendix A will not be resent. The reply period for this Office Action will start from the mailing date of this communication.

2. Applicant's election with traverse of Group I, claims 1-11, with an election of species of SEQ ID NO: 1 in the reply filed on 6/15/2006 is acknowledged. The traversal is on the ground(s) that it would not be an undue burden for the Examiner to search both SEQ ID NO: 1 and SEQ ID NO: 3 as the search for a polynucleotide encoding a protein of SEQ ID NO: 2 would encompass both of the sequences. This is not found persuasive because searching for the nucleotide encoding SEQ ID NO: 2 will only provide the cDNA sequence (SEQ ID NO: 1) and will not provide the genomic sequence of the gene (SEQ ID NO: 3).

The requirement is still deemed proper and is therefore made FINAL. Therefore, claims 12-16 are withdrawn from further consideration. Claims 1-11 are pending and are examined.

Priority

3. Applicant claims benefit to provisional application 60/257175, filed 12/22/2000. However, this application does not contain a sequence of SEQ ID NO: 1 that is 2093 nucleotides long. The SEQ ID NO: 1 disclosed in the provisional application is only 1441 nucleotides long. Therefore, Applicant is entitled to a priority date of 3/14/2001 (filing date of 09/805, 456) with respect to SEQ ID NO: 1, because application 09/805, 456

discloses SEQ ID NO: 1 that is 2093 nucleotides long (identical in size to the instant invention).

Drawings

4. Drawing filed on 10/7/2003 is acknowledged.

Specification

5. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

Claim Objections

6. Claims 1, 6, 10 and 11 are objected to because of the following informalities:

6a. Claims 1, 10 and 11 contains subject matter not elected by the Applicant. Claims 1, 10 and 11 need to be rewritten limiting the reference to the nucleotide of SEQ ID NO: 1 and nucleotide sequence that encodes amino sequence of SEQ ID NO: 2.

6b. Claim 1 is objected to because Applicant's have not followed the correct format ("SEQ ID NO: X") to describe the various sequences.

6c. Claim 6 contains subject matter not elected by the Applicant. Therefore, claim 6 will not be further examined on its merits.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7a. Claim 1 recites the limitation "completely complementary" in the claims. The specification has failed to define the term so as to set forth the meets and bounds of the invention. In addition, the comprising language present in claim (1a) allows for sequences other than SEQ ID NO: 2 to be present in the polypeptide which have not been disclosed in the specification. Therefore, the metes and bounds of the claim are unclear. Claims 2-5 and 7-11 are rejected insofar as they are dependent on rejected claim 1.

7b. Claim 4 is indefinite because the claim recites a recombinant method for producing a polypeptide comprising insertion of the polynucleotide of claim 1(d) into a host cell. Claim 1(d) recite nucleotide sequences that are complementary to nucleotide sequences. It is not clear how the polynucleotide complements of claims 1(a-c) will produce the polypeptide disclosed in the instant application, because the complement is not the coding strand. A complement is a sequence of nucleotide bases in one strand of a DNA or RNA molecule that is exactly complementary (adenine-thymine, adenine-uracil, or guanine-cytosine) to that on another single strand.

Claim Rejections - 35 USC § 101

8. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-5 and 7-11 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

The instant claims are directed to nucleotide sequence that encodes SEQ ID NO: 2 and nucleotide sequence of SEQ ID NO: 1 belonging to a human amino acid transporter protein (page 17). These claims are drawn to an invention with no apparent or disclosed patentable utility. The applicant claims that the protein of the invention is expressed in the testis, brain meningiomas, normal brain, head-neck and colon based on BLAST hits (Figure 1B). In addition, based on tissue screening panels Applicant is able to show expression in human whole liver (Figure 1B). The only experimental data provided on Figure 1 is the nucleotide sequence information and BLAST hits. It also provides the polypeptide sequence in Figure 2A. There are no RNA or protein blots to indicate the expression profile. In addition, the instant application does not disclose the biological role of this protein or its significance. Applicant further asserts that the art has clearly established the commercial importance of members of the transporter family of proteins (page 17). However, Applicant has failed to provide such evidence. In addition, the instant application does not disclose the biological role of this protein or its significance. Novel biological molecules lack well-established utility and must undergo extensive experimentation.

The applicant claims that the human amino acid transporter protein sequence of the instant invention is 476 amino acid long (Figure: 2) and contains structural features

characteristic of transporter protein (Figure: 1B, 2A and page 18, see Boll et al. (2003)). This is presumably because of sequence homology between the instant invention (human transporter protein sequence) and other transporter protein. No function has been ascribed to this transporter protein in the specification (page 19). However, Boll et al. suggest that this amino acid transporter has high selectivity to for amino acids with small side chains (alanine, glycine and proline).

There is little doubt that, after complete characterization, this protein will probably be found to have a patentable utility. This further characterization, however, is part of the act of invention and, until it has been undertaken, Applicant's claimed invention is incomplete. The instant situation is directly analogous to that of which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (Sus. Ct, 1966), in which a novel compound which was structurally analogous to other compounds which were known to possess anticancer activity was alleged to be potentially useful as an antitumor agent in the absence of evidence supporting this utility. The court expressed the opinion that all chemical compounds are "useful" to the chemical arts when this term is given its broadest interpretation. However, the court held that this broad interpretation was not the intended definition of "useful" as it appears in 35 U.S.C. 101, which required that an invention must have either an immediate obvious or fully disclosed "real-world" utility. The court held that:

"The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility," "[u]nless and until a process is refined and developed to this point - where specific benefit exists in currently available form - there is insufficient justification for permitting an applicant to engross what may prove to be a broad field," and "a patent is

not a hunting license," "[i]t is not a reward for the search, but compensation for its successful conclusion."

The instant claims are drawn to nucleotides, which have a yet undetermined function or biological significance. Applicants have disclosed that they are in possession of polypeptide SEQ ID NO: 2 encoded by nucleotides of SEQ ID NO: 1. In addition, Applicant also asserts that the experimental data indicates the expression in the testis, brain meningiomas, normal brain, head-neck tissue, colon and liver (page: 17, Figure 1B). However, there is no actual and specific significance which can be attributed to said polypeptides and the polynucleotides identified in the specification, except the prophetic recitation of potential uses, which include the use of this transporter protein and the nucleotides in screening assays, diagnosing a disease, raise antibodies, tissue markers, binding assays, etc. (pages: 29-64). Mere expression pattern data disclosed fails to indicate what amino acid molecule is being transported or how the transporter is activated. In addition, the specification does not teach what amino acids are transported in which tissues by the claimed invention. Without this information, the skilled artisan would be unable to activate or inhibit the transporter or even know what physiological conditions this process would mediate. Further, there is no nexus with claimed invention and any disease or disorder. For this reason, the instant invention is incomplete. Since neither the prior art nor the specification provides for the physiological significance of the disclosed and claimed amino acid transporter, there is no immediately obvious patentable use for it.

In addition, the instant specification does not disclose a "real-world" use for said polypeptides and polynucleotides, except the prophetic recitation of potential uses,

which include possible biological and therapeutic uses. Also, there are no working examples that demonstrate any specific utility. Thus, the claimed invention is incomplete and, therefore, does not meet the requirements of 35 U.S.C. 101 as being useful.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9a. Claims 1-5 and 7-11 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

9b. Claims 1-5 and 7-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification were it enabling for nucleotide sequence of SEQ ID NO: 1 or nucleotide sequence encoding SEQ ID NO: 2 as described in Figure 1A, does not reasonably provide enablement for all possible variants including those that are at least 80% or 90% identical to SEQ ID NO: 1 contemplated by the Applicant. The claims also recite the phrases "a nucleotide sequence" and " a peptide " and thus, are broadly interpreted by the Examiner as reading upon: (i) DNA and protein variants with any number of deletions, substitutions, or additions and (ii) fragments of SEQ ID NOs: 1-2, including sequences only 8 amino acids or 12 nucleic acids in length (see specification page 27 and page 44). The specification does not enable any person skilled in the art to

which it pertains, or with which it is most nearly connected, to make and use the invention as claimed.

The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. See *In re Wands,* 858 F.2d at 737, 8 USPQ2d at 1404. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The instant claims reads on nucleotide sequence variants including those that are at least 80% or 90% identical to SEQ ID NO: 1. The claims also recite the phrases "a nucleotide sequence" and " a peptide " and thus, are broadly interpreted by the Examiner as reading upon: (i) DNA and protein variants with any number of deletions, substitutions, or additions and (ii) fragments of SEQ ID NOs: 1-2, including sequences only 8 amino acids or 12 nucleic acids in length (see specification page 27 and page 44). In addition, Applicant has not defined in the specification if "completely complementary" describes a full-length complementary sequence and thus the Examiner has interpreted it to include fragments that are at least 12 nucleic acids long.

However, other than the nucleic acid sequence of SEQ ID NO: 1 and nucleic acid encoding polypeptide of SEQ ID NO: 2, the specification as filed fails to disclose any other nucleic acid sequence recited in the instant claim. The specification does not teach functional or structural characteristics of the polypeptide variants, fragments, and derivatives encompassed by the claims.

Despite knowledge in the art for producing variant polynucleotide that encode polypeptides, the specification fails to provide any guidance regarding the variant polynucleotide sequences encoding the polypeptides by the contemplated methods that retain the function. Furthermore, detailed information regarding the structural and functional requirements of the disclosed protein is lacking. Although it is accepted that the amino acid sequence of a polypeptide determines its structural and functional properties, predicting a protein's structure and function from mere sequence data remains an elusive task. The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no

substitutions (see Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure Prediction, pp. 492-495). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active variants, this is not adequate guidance as to the nature of active derivatives that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity. Therefore, predicting which polypeptide, if any, would retain the functions of the protein is well outside the realm of routine experimentation. Further, since no function has been attributed to the claimed protein, the skilled artisan would not know what function to test for. Thus, an undue amount of experimentation would be required to generate the changes/modifications contemplated and yet retain the function of the proteins claimed.

Applicant has not taught how one of skill in the art would use the full scope of polynucleotide sequences encompassed by the invention of claims 1-5 and 7-11. The

specification as filed does not sufficiently teach one of skill in the art how to make and/or use the full scope of the claimed sequences. The amount of experimentation required to make and/or use the full scope of the claimed sequences would require trial and error experimentation to determine the functional sequences.

Given the breadth of claims 1-5 and 7-11 in light of the unpredictability of the art as determined by the lack of working examples and shown by the prior at of record, the level of skill of the artisan, and the lack of guidance provided in the instant specification, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

9c. Claims 3 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated or cultured cell comprising an expression vector, does not reasonably provide enablement for a host cell comprising an expression vector. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The Examiner has interpreted the claim 3 as reading on isolated host cells, as well as host cells in the context of a multicellular, transgenic organism and host cells intended for gene therapy. The specification of the instant application teaches that amino acid transporter gene products (SEQ ID NO: 1) can be expressed in transgenic animals and any technique known in the art may be used to introduce a amino acid transporter transgene into animals to produce the founder lines of transgenic animals (pages 62-64). However, there are no methods or working examples disclosed in the

instant application whereby a multicellular animal with the incorporated amino acid transporter gene of SEQ ID NO: 1 is demonstrated to express the amino acid transporter peptide of the instant invention. There are also no methods or working examples in the specification indicating that a multicellular animal has amino acid transporter "knocked out". The unpredictability of the art is *very high* with regards to making transgenic animals. For example, Wang et al. (Nuc. Acids Res. 27: 4609-4618, 1999; pg 4617) surveyed gene expression in transgenic animals and found in each experimental animal with a single "knock-in" gene, multiple changes in genes and protein products, often many of which were unrelated to the original gene. Likewise, Kaufman et al (Blood 94: 3178-3184, 1999) found transgene expression levels in their transfected animals varied from "full" (9 %) to "intermediate" to "none" due to factors such as "vector poisoning" and spontaneous structural rearrangements (pg 3180, col 1, 2nd full paragraph; pg 3182-3183). Additionally, for example, the specification discloses that two possible techniques used to introduce an amino acid transporter transgene into animals include pronuclear microinjection and gene targeting in embryonic stem cells. However, the literature teaches that the production of transgenic animals by microinjection of embryos suffers from a number of limitations, such as the extremely low frequency of integration events and the random integration of the transgene into the genome which may disrupt or interfere with critical endogenous gene expression (Wigley et al. Reprod Fert Dev 6: 585-588, 1994). The inclusion of sequences that allow for homologous recombination between the transgenic vector and the host cell's genome does not overcome these problems, as homologous recombination events are

even rarer than random events. Therefore, in view of the extremely low frequency of both targeted and non-targeted homologous recombination events in microinjected embryos, it would have required undue experimentation for the skilled artisan to have made any and all transgenic non-human animals according to the instant invention. Furthermore, regarding gene targeting in embryonic stem cells, the specification does not provide guidance for identifying and isolating embryonic stem cells or for identifying other embryonal cells which are capable of contributing to the germ line of any animal. At the time of filing, Campbell et al. teaches that, "in species other than the mouse the isolation of ES cells has proved more difficult. There are reports of ES-like cell lines in a number of species...However, as yet there are not reports of any cell lines which contribute to the germ line in any species other than mouse" (Campbell et al. Theriology 47(1): 63-72, 1997; see pg 65, 2nd paragraph). Thus, based on the art recognized unpredictability of isolating and using embryonic stem cells or other embryonal cells from animals other than mice to produce transgenic animals, and in view of the lack of guidance provided by the specification for identifying and isolating embryonal cells which can contribute to the germ line of any non-human mammal other than the mouse, such as dogs or cows, the skilled artisan would not have had a reasonable expectation of success in generating any and all non-human transgenic animals using ES cell technology.

The specification also discloses "the nucleic acid molecules also provide vectors for gene therapy in patients containing cells that are aberrant in transporter gene expression. Thus, recombinant cells, which include the patient's cells that have been

engineered *ex vivo* and returned to the patient, are introduced into an individual where the cells produce the desired transporter protein to treat the individual" (page 52). However, the specification does not teach any methods or working examples that indicate an amino acid transporter nucleic acid is introduced and expressed in a cell for therapeutic purposes. The disclosure in the specification is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. For example, the specification does not teach what type of vector would introduce the amino acid transporter nucleic acid into the cell or in what quantity and duration. Relevant literature teaches that since 1990, about 3500 patients have been treated via gene therapy and although some evidence of gene transfer has been seen, it has generally been inadequate for a meaningful clinical response (Phillips, A., J Pharm Pharmacology 53: 1169-1174, 2001; abstract). Additionally, the major challenge to gene therapy is to deliver DNA to the target tissues and to transport it to the cell nucleus to enable the required protein to be expressed (Phillips, A.; pg 1170, ¶ 1). Phillips also states that the problem with gene therapy is two-fold: 1) a system must designed to deliver DNA to a specific target and to prevent degradation within the body, and 2) an expression system must be built into the DNA construct to allow the target cell to express the protein at therapeutic levels for the desired length of time (pg 1170, ¶ 1). Therefore, undue experimentation would be required of the skilled artisan to introduce and express an amino acid transporter nucleic acid into the cell of an organism. Additionally, gene therapy is unpredictable and complex wherein one skilled in the art may not necessarily

be able to introduce and express an amino acid transporter nucleic acid in the cell of an organism or be able to produce an amino acid transporter protein in that cell.

Due to the large quantity of experimentation necessary to generate a transgenic animal expressing the amino acid transporter protein and to introduce and express an amino acid transporter nucleic acid in a cell of an organism for therapy, the lack of direction/guidance presented in the specification regarding how to introduce an amino acid transporter nucleic acid in the cell of an organism to be able produce that amino acid transporter, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of making transgenic animals and the unpredictability of transferring genes into an organism's cells, and the breadth of the claims which fail to recite any cell type limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope. (Please note that this issue could be overcome by amending the claims to recite, for example, "An isolated host cell...").

9d. Claims 1-5 and 7-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *This is a written description rejection.*

The specification discloses the nucleotide sequence of SEQ ID NO: 1 (Figure: 1A) and nucleotide sequence encoding SEQ ID NO: 2. This meets the written

description provisions of 35 USC 112, first paragraph. However, the specification does not disclose all possible variants all possible variants including those that are at least 80% or 90% identical to SEQ ID NO: 1 contemplated by the Applicant. The claims also recite the phrases "a nucleotide sequence" and " a peptide " and thus, are broadly interpreted by the Examiner as reading upon: (i) DNA and protein variants with any number of deletions, substitutions, or additions and (ii) fragments of SEQ ID NOs: 1-2, including sequences only 8 amino acids or 12 nucleic acids in length (see specification page 27 and page 44). In addition, Applicant has not defined in the specification if "completely complementary" describes a full-length complementary sequence and thus the Examiner has interpreted it to include fragments that are at least 12 nucleic acids long.

The claims as written, however, encompass variant sequences which were not originally contemplated and fail to meet the written description provision of 35 USC 112, first paragraph because the written description is not commensurate in scope with the recitation of claims 1-5 and 7-11. The specification does not provide written description to support the genus encompassed by the instant claims.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (*See Vas-Cath* at page 1116).

With the exception of isolated nucleotide sequence of SEQ ID NO: 1 (Figure: 1A) and nucleotide sequence encoding SEQ ID NO: 2, the skilled artisan cannot envision all

the detailed chemical structure of the claimed polynucleotide sequences of the variants regardless of the complexity or simplicity of the method of isolation.

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The polypeptide itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes v. Baird*, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

Therefore, only the isolated nucleotide sequence of SEQ ID NO: 1 (Figure: 1A) and nucleotide sequence encoding SEQ ID NO: 2 but not the full breadth of the claims meets the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. As a result, it does not appear that the inventors were in possession of various polynucleotide sequences set forth in claims 1-5 and 7-11.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.) Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent

> granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10a. Claims 1-5 and 7-11 rejected under 35 U.S.C. 102(e) as being anticipated by Tang et al. (U. S. Patent No. 6, 743, 619).

Claims are drawn to isolated nucleic acids. The claims also recite the phrases "a nucleotide sequence" and " a peptide " and thus, are broadly interpreted by the Examiner as reading upon: (i) DNA and protein variants with any number of deletions, substitutions, or additions and (ii) fragments of SEQ ID NOs: 1-2, including sequences only 12 nucleic acids or 8 amino acids in length (see specification page 44 and page 27). In addition, Applicant has not defined in the specification if "completely complementary" describes a full-length complementary sequence and thus the Examiner has interpreted it to include fragments that are at least 12 nucleic acids long.

Tang et al. discloses nucleic acid sequence (SEQ ID NO: 9) that has an overall identity of 71.6% to SEQ ID NO: 1 of the instant invention. Further, it has greater than 99.9% identity to nucleotides 103-1602 of SEQ ID NO: 1 of the instant invention (see Appendix A1-2). It is also noted that SEQ ID NO: 1 is 2093 nucleotides long. Thus, the reference anticipates the various variants and fragments of the instant invention. Tang et al. also discloses vectors, host cells and method of making proteins (column 15-20). Therefore, claims 1-5 and 7-11 are rejected as being anticipated by Tang et al. (U. S. Patent No. 6, 743, 619).

Conclusion

11. No claims are allowed.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jegatheesan Seharaseyon, Ph.D whose telephone number is 571-272-0892. The examiner can normally be reached on M-F: 8:30-5:00. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JS
Art Unit 1647,
October 29, 2006

Jegatheesan Seharaseyon
Patent Examiner